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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,751

05/03/2007

Liang Li

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EXAMINER

NATARAJAN, MEERA

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,751	Applicant(s) LI ET AL.	
	Examiner MEERA NATARAJAN	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) 1, 2 and 6-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3 is/are rejected.
- 7) ☒ Claim(s) 4 and 5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/03/2007 and 06/14/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, Claims 3-5 in the reply filed on 07/14/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 1, 2, 6-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/14/2008.
3. Claims 3-5 will be examined on the merits.

Claim Objections

4. Claims 3-5 are objected to because of the following informalities: There are several abbreviations in the claims however each abbreviation should be spelled out first, at least once, and then can be referred to with appropriate abbreviation. For example, Claim 1 recites "lidamycin" without any specified abbreviation, however dependent Claim 3b recites "LDM". Appropriate correction is required.
5. Claims 3-5 are objected to for depending on non-elected claims. Claim 1 has been withdrawn as being drawn to a non-elected invention. Therefore the elected claims must be written in independent form and cannot depend on a non-elected claim. Correction is required. For examination purposes, the claims will be examined with the limitations of Claim 1.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 3, step b recites the term "LDM". It is unclear what is meant by LDM. Clarification is required.

9. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 5 recites the term "preferably" 90%. The relative degree of preferably is unclear and therefore the metes and bounds of the claim are indefinite. Clarification is required.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (*Acta Pharmaceutica Sinica*, Vol. 35, No.7, pp.488-491, 2000) in view of Terpe et al. (*Appl. Microbiol. Biotechnol.*, Vol. 60, pp.523-533, epub Nov. 2002).

14. The claim is drawn to a method of producing an energized fusion protein Fv-LDP-AE consisting of a fusion protein Fv-LDP that contains the single-chain Fv fragment (scFv) of monoclonal antibody against type IV collagenase, the apoprotein of lidamycin (LDP), the flexible spacer GGGGS between scFv and LDP, and a C-terminal His₆-tag and an active enediyne chromophore (AE) that derives from lidamycin.

15. Li et al teach engineering and assembling a fusion protein consisting of a enediyne chromophore of lidamycin (see Fig.1 and materials and methods) and a recombinant fusion protein LDP-Fv which comprises a scFv antibody against type IV collagenase, lida-protein(LDP) and the spacer GGGGS between them. Li et al. teach anti-invasion activity of the LDP-Fv fusion protein in lung cancer PG cells (see Fig. 5). Li et al. does not teach a His₆-tag. This deficiency is made up for by Terpe et al.

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16. Terpe et al. teach proteins containing a tag to facilitate the purification of the target polypeptides are widely used. Terpe et al. disclose several tags such as FLAG-tag, HAT-tag, His-tag, Strep-tag and S-tag (see abstract).

17. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use a His-tag as taught by Terpe et al. to help in the purification of the fusion protein taught by Li et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the teachings of Li et al. and Terpe et al., because Terpe et al. teach tag, specifically His-tags, facilitate purification of the target polypeptides and are most commonly used. Although Li et al. is silent in regards to the percentage of enediyne chromophore (AE), the fusion protein was used in an anti-invasion assay of lung cancer cells and therefore one of ordinary skill in the art would be motivated to optimize the percentage of AE by routine experimentation in order to achieve the best cytotoxicity because Li et al. teach use of the fusion protein in cancer therapy.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

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F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 3-5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of copending Application No. 11/587199. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to a method of producing the same fusion protein. The instant application claims are described above. Claim 4 of application 11/587199 is drawn to a method for producing a single domain antibody energized fusion protein comprising a fusion protein VH-LDP that contain the heavy chain variable domain VH of monoclonal antibody 3G11 against type IV collagenase, the flexible spacer GGGGS, the apoprotein of lidamycin (LDP) and a His₆-tag and an active enediyne chromophore (AE). The instant claims are broadly drawn to a single-chain Fv fragment of a monoclonal antibody against type IV collagenase and therefore the antibody of claim 4 of application 11/587199 falls within the same scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

20. Claim 3-5 are rejected.

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21. No Claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643